

08/907,041

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(FILE 'HOME' ENTERED AT 19:24:47 ON 01 DEC 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 19:25:55 ON 01 DEC 2003

L1 148987 S GLUTAMYL(W) TRANSPEPTIDASE OR GLUTATHIONE(W) PEROXIDASE OR CATA  
L2 148673 S METALLOTHIONASE OR SUPEROXIDE(W) DISMUTASE OR BLEOMYCIN(W) HYDR  
L3 251264 S L1 OR L2  
L4 2798 S L3 (6A) (DNA OR POLYNUCLEOTIDE OR NUCLEIC(W) ACID)  
L5 8679 S PROTECT? (10A) (TOXIC(W) SPECIES OR FREE(W) RADICAL OR SUPEROXIDE  
L6 14 S L4 AND L5  
L7 11 DUP REM L6 (3 DUPLICATES REMOVED)

=> d bib ab 1-11 17

L7 ANSWER 1 OF 11 MEDLINE on STN DUPLICATE 1  
AN 2002445359 MEDLINE  
DN 22112975 PubMed ID: 12117500  
TI Cloning, production and characterisation of a recombinant Cu/Zn superoxide  
dismutase from Taenia solium.  
AU Castellanos-Gonzalez Alejandro; Jimenez Lucia; Landa Abraham  
CS Departamento de Microbiologia y Parasitologia, Facultad de Medicina,  
Edificio A, 2do piso, Universidad Nacional Autonoma de Mexico, Ciudad  
Universitaria, Mexico D.F. 04510, Mexico.  
SO INTERNATIONAL JOURNAL FOR PARASITOLOGY, (2002 Aug) 32 (9) 1175-82.  
Journal code: 0314024. ISSN: 0020-7519.  
CY England: United Kingdom  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
OS GENBANK-AF439353  
EM 200211  
ED Entered STN: 20020904  
Last Updated on STN: 20021212  
Entered Medline: 20021114  
AB A full-length complementary **DNA** clone encoding a cytosolic Cu/Zn  
**superoxide dismutase** with a M(r) of 15,588 Da was  
isolated from a Taenia solium larvae complementary DNA library.  
Comparison analysis of its deduced amino acid sequence revealed a 71%  
identity with Schistosoma mansoni, 57.2-59.8% with mammalian and less than  
54% with other helminth cytosolic Cu/Zn superoxide dismutase. The  
characteristic motifs and the amino acid residues involved in coordinating  
copper and zinc enzymatic function are conserved. The T. solium Cu/Zn  
superoxide dismutase was expressed in the pRSET vector. Enzymatic and  
filtration chromatographic analysis showed a recombinant enzyme with an  
activity of 2,941 U/mg protein and a native M(r) of 37 kDa. Inhibition  
assays using KCN, H(2)O(2), NaN(3) and SDS indicated that Cu/Zn is the  
metallic cofactor in the enzyme. Thiabendazole (500 microM) and  
albendazole (300 microM) completely inhibited the activity of T. solium  
Cu/Zn superoxide dismutase. Thiabendazole had no effect on bovine Cu/Zn  
superoxide dismutase; in contrast, albendazole had a moderate effect on it  
at same concentrations. Antibodies against T. solium Cu/Zn superoxide  
dismutase did not affect the enzymatic function; nevertheless, it cross  
reacts with several Taenia species, but not with trematodes, nematodes,  
pig, human and bovine Cu/Zn superoxide dismutase enzymes. Western blot  
analysis indicated the enzyme was expressed in all stages. These results  
indicate that T. solium possesses a Cu/Zn superoxide dismutase enzyme that  
can **protect** him from oxidant-damage caused by the  
**superoxide anion**.  
  
L7 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2003 ACS on STN  
AN 2002:177838 CAPLUS

DN 136:290312  
 TI Melatonin reduces phosphine-induced lipid and DNA oxidation in vitro and in vivo in rat brain  
 AU Hsu, Ching-Hung; Chi, Bei-Ching; Casida, John E.  
 CS Department of Public Health, School of Medicine, Taipei Medical University, Taipei, Taiwan  
 SO Journal of Pineal Research (2002), 32(1), 53-58  
 CODEN: JPRSE9; ISSN: 0742-3098  
 PB Blackwell Munksgaard  
 DT Journal  
 LA English  
 AB Phosphine (PH3), a widely used pesticide, was found in our recent study to induce oxidative damage in the brain, liver and lung of rats. We also obsd. that melatonin significantly blocked this action. The present study focused on brain and the magnitude and mechanism of protection of PH3-induced oxidative damage by melatonin in vitro and in vivo. PH3 in whole brain homogenate (3 mg protein/mL Tris-HCl pH 7.4 buffer) induced increasing lipid peroxidn. [as malondialdehyde (MDA) and 4-hydroxyalkenals (4-HDA)] dependent on concn. (0.25-2 mM) and time (30-150 min), reaching a max. level of 2.9-fold at 90 min after PH3 at 1 mM. Elevation of MDA + 4-HDA levels by PH3 at 1 mM was also obsd. in homogenates of cerebral cortex, cerebellum, hippocampus and hypothalamus examd. individually. Melatonin at 0.1-2 mM progressively inhibited PH3-induced lipid peroxidn. in brain and regions thereof. Addnl., PH3 induced brain DNA oxidn. in vitro and in vivo detd. as 8-hydroxyguanosine (8-OH-dG). Melatonin at 1 mM significantly suppressed PH3-induced brain DNA oxidn. in vitro. PH3 at 4 mg/kg i.p. significantly elevated 8-OH-dG in frontal cortex and melatonin prevented it. PH3 in vivo marginally lowered brain glutathione peroxidase activity and melatonin restored it completely. In contrast, PH3 and melatonin both stimulated superoxide dismutase prodn. Brain glutathione (GSH) levels in PH3-treated rats were significantly reduced at 30 min and recovered gradually. It is concluded that melatonin, probably because of its **free radical** scavenging ability, confers marked **protection** against PH3-induced oxidative toxicity in brain.

RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2003 ACS on STN  
 AN 2000:910778 CAPLUS  
 DN 134:176857  
 TI Metallothionein inhibits peroxynitrite-induced DNA and lipoprotein damage  
 AU Cai, Lu; Klein, Jon B.; Kang, Y. James  
 CS Department of Medicine, University of Louisville, Louisville, KY, 40292, USA  
 SO Journal of Biological Chemistry (2000), 275(50), 38957-38960  
 CODEN: JBCHA3; ISSN: 0021-9258  
 PB American Society for Biochemistry and Molecular Biology  
 DT Journal  
 LA English  
 AB Previous studies have demonstrated that metallothionein functions as an antioxidant that **protects** against oxidative DNA, protein, and lipid damage induced by **superoxide anion**, hydrogen peroxide, hydroxyl radical, and nitric oxide. The present study was undertaken to test the hypothesis that metallothionein also protects from DNA and lipoprotein damage induced by peroxynitrite, an important reactive nitrogen species that causes a diversity of pathol. processes. A cell-free system was used. DNA damage was detected by the mobility of plasmid DNA in electrophoresis. Oxidn. of low d. lipoprotein was measured by a thiobarbituric acid-reactive substance, which was confirmed by lipid hydroperoxide assay. Plasmid DNA damage and low d. lipoprotein oxidn. were induced by 3-morpholiniosydnomine, which produces peroxynitrite through the reaction between nitric oxide and superoxide anion or by synthesized peroxynitrite directly. DNA damage by 3-morpholiniosydnomine

was prevented by both metallothionein and superoxide dismutase, whereas the damage caused by peroxynitrite was prevented by metallothionein only. The oxidn. of low d. lipoprotein by 3-morpholinosydnomine and peroxynitrite was also significantly inhibited by metallothionein. This study thus demonstrates that metallothionein may react directly with peroxynitrite to prevent DNA and lipoprotein damage induced by this pathol. reactive nitrogen species.

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2003 ACS on STN  
AN 1999:617858 CAPLUS  
DN 132:164494  
TI Local hypomethylation in atherosclerosis found in rabbit ec-sod gene  
AU Laukkanen, Mikko O.; Mannermaa, Sanna; Hiltunen, Mikko O.; Aittomaki, Saara; Airenne, Kari; Janne, Juhani; Yla-Herttuala, Seppo  
CS A. I. Virtanen Institute, University of Kuopio, Kuopio, 70211, Finland  
SO Arteriosclerosis, Thrombosis, and Vascular Biology (1999), 19(9), 2171-2178  
CODEN: ATVBFA; ISSN: 1079-5642  
PB Lippincott Williams & Wilkins  
DT Journal  
LA English  
AB Extracellular superoxide dismutase (EC-SOD) **protects** arteries against deleterious effects of **superoxide anions** and the development of atherosclerosis. In this study, the authors cloned and characterized rabbit ec-sod gene. The authors identified 6 rabbit C-elements and 5 CpG clusters in the cloned sequence. One of the CpG clusters is located on the coding sequence. Because CpG clusters are potential sites for methylation and may explain the occurrence of mutations, methylation status of each of the CpG dimers located in the coding sequence CpG cluster was characterized using direct genomic sequencing. Unexpectedly, a marked redn. in the amt. of methylated CpG dinucleotides in ec-sod gene was detected in atherosclerotic aortas as compared with normal aortic intima-media. Although alterations in DNA methylation are well characterized in malignant tumors, the presence of methylation changes in atherosclerosis has not been studied even though both diseases are characterized by excess cellular proliferation and alterations in gene expression. Further anal. of the whole genomic methylation by high-pressure liq. chromatog. in normal and atherosclerotic aortas revealed a tendency for a decreased 5-methylcytosine (5-mC) content in atherosclerotic aortas as compared with normal arteries. Hypomethylation in atherosclerotic aortas occurred at the same level as has been reported from malignant tumors. Although a causal relation between the methylation level and expression of EC-SOD cannot be proven, the results show that ec-sod hypomethylation is assocd. with the development of atherosclerosis and suggest that it may affect structure and function of ec-sod and other genes possibly involved in the development of atherosclerotic lesions.

RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 11 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
AN 2000:2085 BIOSIS  
DN PREV200000002085  
TI Effects of secreted SOD delivered by genetically modified cells on xanthine/xanthine oxidase and paraquat-induced cytotoxicity in vitro.  
AU Komada, Fusao [Reprint author]; Nishiguchi, Kohshi; Tanigawara, Yusuke; Iwakawa, Seigo; Okumura, Katsuhiko  
CS Department of Hospital Pharmacy, School of Medicine, Kobe University, Kusunoki-cho, Chuo-ku, Kobe, 650-0017, Japan  
SO Biological and Pharmaceutical Bulletin, (Aug., 1999) Vol. 22, No. 8, pp. 846-853. print.  
ISSN: 0918-6158.

DT Article  
 LA English  
 ED Entered STN: 23 Dec 1999  
 Last Updated on STN: 31 Dec 2001  
 AB We designed a new eukaryotic expression vector for secretable superoxide dismutase (SOD), which expresses human SOD cDNA by fusing it to 1 connecting amino acid and the signal peptide DNA sequence of the human interleukin-2 (IL-2) gene (IL-SOD(2) cDNA). The ILSOD(2) cDNA constructed by PCR-based gene expression was ligated into the multicloning site of the pRc/CMV plasmid (pRc/CMV-ILSOD(2)). Rat lung epithelial-like cells (L2 cells) and rat skin fibroblasts (FR cells) were transfected with pRc/CMV-ILSOD(2) by lipofection. The extracellular SOD activities of IS(2)-L2 cells (L2 cells transfected with pRc/CMV-ILSOD(2)) and IS(2)-FR cells (FR cells transfected with pRc/CMV-ILSOD(2)) were 2-3 times higher than those of host cells. Initially, we investigated the protective effect of extracellular SOD secreted from these transformed cells (IS(2)-L2 and IS(2)-FR cells) on extracellular superoxide anion (xanthine/xanthine oxidase; X/XO treatment)-induced cytotoxicity in normal cells. The sensitivities of these transformed cells to X/XO-induced cytotoxicity was decreased significantly as compared with that of host cells. Although, the conditioned medium from IS(2)-L2 and IS(2)-FR cells protected against X/XO-induced cytotoxicity, the conditioned medium from host cells (L2 and FR cells) showed no significant effects on X/XO-induced cytotoxicity. Furthermore, the conditioned medium from transformed cells was more effective than that of host cells against lipid peroxidation by normal cells under conditions of oxidative stress. Second, we generated superoxide anions in the intracellular space by paraquat treatment. The transformed cells were more sensitive to paraquat-induced cytotoxicity than host cells. Following addition of catalase, the sensitivity of these genetically modified cells to paraquat became equivalent to that of host cells. These results indicated a **protective** effect of transfection with secretable SOD genes against extracellular **superoxide anion**-induced cytotoxicity although no such **protective** effect was observed against the intracellular cytotoxicity generated by paraquat treatment.

L7 ANSWER 6 OF 11 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
 AN 1998:125273 BIOSIS  
 DN PREV199800125273  
 TI Cloning, characterization and overexpression of two iron superoxide dismutase cDNAs from *Leishmania chagasi*: Role in pathogenesis.  
 AU Paramchuk, Wendy J.; Ismail, Said O.; Bhatia, Ajay; Gedamu, Lashitew [Reprint author]  
 CS Dep. Biol. Sci., Univ. Calgary, Calgary, AB T2N 1N4, Canada  
 SO Molecular and Biochemical Parasitology, (Dec. 1, 1997) Vol. 90, No. 1, pp. 203-221. print.  
 CODEN: MBIPDP. ISSN: 0166-6851.  
 DT Article  
 LA English  
 ED Entered STN: 5 Mar 1998  
 Last Updated on STN: 6 Apr 1998  
 AB We have isolated and characterized two superoxide dismutase (SOD) cDNAs from a *Leishmania chagasi* promastigote cDNA library using degenerate primers derived from conserved amino acid residues of previously isolated manganese and iron SODs. Comparison of these two *L. chagasi* SOD deduced amino acid sequences with previously isolated MnSOD and FeSOD amino acid sequences revealed that they have higher homology to, and complete conservation of, invariant residues found in iron-containing SODs. Southern blot analysis showed that one gene, *L.c.FeSODA*, is a single copy gene, whereas the other gene, *L.c.FeSODB*, belongs to a multi-gene family. Transcript levels and enzyme activities of *L.c.FeSODA* and *L.c.FeSODB* show differential stage expression, with higher levels present in the amastigote stage of the parasite compared to the promastigote stage. Expression of the *L.c.FeSODs* in an *E. coli* SOD null strain

**protected** the bacteria against **free radical** generating agents. Overexpression of these FeSODs in *L. chagasi* parasites also showed enhanced **protection** against the **free radical** generating agents, paraquat and nitroprusside. The cloning, characterization and overexpression of the *L.c.FeSODA* and *L.c.FeSODB* genes and proteins demonstrates the possible role of SODs in *Leishmania* pathogenesis.

L7 ANSWER 7 OF 11 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN  
 AN 97:457076 SCISEARCH  
 GA The Genuine Article (R) Number: XC834  
 TI Use of the comet assay to investigate possible interactions of nitric oxide and reactive oxygen species in the induction of DNA damage and inhibition of function in an insulin-secreting cell line  
 AU Delaney C A; Green I C; Lowe J E; Cunningham J M; Butler A R; Renton L; DCosta I; Green M H L (Reprint)  
 CS UNIV SUSSEX, MRC, CELL MUTAT UNIT, BRIGHTON BN1 9RR, E SUSSEX, ENGLAND (Reprint); UNIV SUSSEX, MRC, CELL MUTAT UNIT, BRIGHTON BN1 9RR, E SUSSEX, ENGLAND; UNIV SUSSEX, SCH BIOL SCI, BIOCHEM LAB, BRIGHTON BN1 9QG, E SUSSEX, ENGLAND; UNIV ST ANDREWS, DEPT CHEM, ST ANDREWS KY16 9ST, FIFE, SCOTLAND  
 CYA ENGLAND; SCOTLAND  
 SO MUTATION RESEARCH-FUNDAMENTAL AND MOLECULAR MECHANISMS OF MUTAGENESIS, (29 APR 1997) Vol. 375, No. 2, pp. 137-146.  
 Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.  
 ISSN: 0027-5107.  
 DT Article; Journal  
 FS LIFE  
 LA English  
 REC Reference Count: 63  
 \*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*  
 AB We have previously used the comet assay to demonstrate that the nitric oxide donor 3-morpholiniosydnonimine (SIN-1) produces DNA damage in rat islets of Langerhans and in the SV40-transformed insulin-secreting hamster cell line, HIT-T15. Damage is not prevented by the addition of superoxide dismutase (SOD). In the present study, we have compared SIN-1, which generates nitric oxide, superoxide anion and hydrogen peroxide, with two other nitric oxide donors, S-nitrosoglutathione (GSNO) and the tetra-iron-sulphur cluster nitrosyl, Roussin's black salt (RES). We have used the comet assay as a highly sensitive method to measure DNA-damaging ability, and also measured inhibition of DNA synthesis and inhibition of insulin secretion. We have examined the effect of SOD and catalase on each of these endpoints in HIT-T15 cells following a 30-min exposure to the compounds (24 h for DNA synthesis). All compounds produced a significant dose-dependent increase in strand-breakage formation and all inhibited DNA synthesis and glucose-stimulated insulin secretion. RES was the most potent. SOD did not reduce the responses observed with any of the compounds. **Catalase** largely prevented **DNA** strand breakage, inhibition of DNA synthesis and inhibition of insulin secretion by SIN-1, but had no effect on responses to GSNO or RES. Addition of SOD together with catalase gave no greater **protection** against SIN-1 than catalase alone. The nitric oxide and **superoxide anion** produced by SIN-1 are thought to combine to form highly reactive peroxynitrite. In addition, H<sub>2</sub>O<sub>2</sub> may be formed in the presence of SIN-1 and may form hydroxyl radical in the presence of a transition metal, such as Fe<sup>2+</sup>. It appears that in insulin-secreting cells, the effects of SIN-1 are largely mediated by this latter mechanism. In contrast, GSNO and RES appear to act by a different mechanism, not overtly involving reactive oxygen species. GSNO and H<sub>2</sub>O<sub>2</sub> show no significant interaction in the induction of DNA strand breaks. Both nitric oxide and H<sub>2</sub>O<sub>2</sub> are effective, directly or indirectly, as DNA strand-breaking agents, inhibitors of DNA synthesis and inhibitors of insulin secretion.

L7 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2003 ACS on STN  
AN 1996:600804 CAPLUS  
DN 125:268872  
TI DNA and RNA strand scission by copper, zinc and manganese superoxide  
dismutases  
AU Dowjat, W. Karol; Kharatishvili, Malkhaz; Costa, Max  
CS Nelson Institute of Environmental Medicine, New York University Medical  
Center, New York, NY, 10987, USA  
SO BioMetals (1996), 9(4), 327-335  
CODEN: BOMEHH; ISSN: 0966-0844  
PB Rapid Science Publishers  
DT Journal  
LA English  
AB Copper/zinc (Cu/ZnSOD) and manganese (MnSOD) superoxide dismutases which  
catalyze the dismutation of toxic **superoxide anion**,  
O<sub>2</sub><sup>-</sup>, to O<sub>2</sub> and H<sub>2</sub>O<sub>2</sub>, play a major role in **protecting** cells from  
toxicity of oxidative stress. However, cells overexpressing either form  
of the enzyme show signs of toxicity, suggesting that too much SOD may be  
injurious to the cell. To elucidate the possible mechanism of this  
cytotoxicity, the effect of SOD on DNA and RNA strand scission was  
studied. High purity preps. of Cu/ZnSOD and MnSOD were tested in an in  
vitro assay in which DNA cleavage was measured by conversion of  
phage.ϕphi.X174 supercoiled double-stranded DNA to open circular and  
linear forms. Both types of SOD were able to induce DNA strand scission  
generating single- and double-strand breaks in a process that required  
oxygen and the presence of fully active enzyme. The DNA strand scission  
could be prevented by specific anti-SOD antibodies added directly or used  
for immunodepletion of SOD. Requirement for oxygen and the effect of  
Fe(II) and Fe(III) ions suggest that cleavage of DNA may be in part  
mediated by hydroxyl radicals formed in Fenton-type reactions where  
enzyme-bound transition metals serve as a catalyst by first being reduced  
by superoxide and then oxidized by H<sub>2</sub>O<sub>2</sub>. Another mechanism was probably  
operative in this system, since in the presence of magnesium DNA cleavage  
by SOD was oxygen independent and not affected by sodium cyanide. It is  
postulated that SOD, by having a similar structure to the active center of  
zinc-contg. nucleases, is capable of exhibiting non-specific nuclease  
activity causing hydrolysis of the phosphodiester bonds of DNA and RNA.  
Both types of SOD were shown to effectively cleave RNA. These findings  
may help explain the origin of pathol. of certain hereditary diseases  
genetically linked to Cu/ZnSOD gene.

L7 ANSWER 9 OF 11 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN  
AN 93:715859 SCISEARCH  
GA The Genuine Article (R) Number: MJ387  
TI EXPRESSION OF HUMAN CATALASE IN ACATALASEMIC MURINE SV-B(2) CELLS CONFERS  
PROTECTION FROM OXIDATIVE DAMAGE  
AU LINDAUSHEPARD B A (Reprint); SHAFFER J B  
CS NEW YORK STATE DEPT HLTH, WADSWORTH CTR LABS & RES, POB 509, ALBANY, NY,  
12201 (Reprint); SUNY ALBANY, SCH PUBL HLTH, ALBANY, NY, 12222  
CYA USA  
SO FREE RADICAL BIOLOGY AND MEDICINE, (DEC 1993) Vol. 15, No. 6, pp. 581-588.  
ISSN: 0891-5849.  
DT Article; Journal  
FS LIFE  
LA ENGLISH  
REC Reference Count: 26  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*  
AB Reactive oxygen species have been implicated in aerobic organisms as  
causative agents in damage to **DNA**, proteins, and lipids.  
**Catalase** is a major enzyme in the defense against such oxidant  
damage. To determine whether increased catalase expression confers greater  
resistance to oxidant stress, a eukaryotic expression vector harboring a  
human catalase cDNA clone was constructed. Acatlasemic murine fibroblasts  
were then co-transfected with the catalase expression vector and pSV2-neo,

and successfully transfected cells were identified by their ability to grow in the presence of geneticin. Clones that contained integrated copies of the catalase expression vector were identified by Polymerase Chain Reaction (PCR) analysis. Stably transfected geneticin-resistant cell lines that overexpressed catalase in potentially positive cell lines were confirmed by catalase enzyme assays. To examine the physiological relevance of catalase overexpression, cells were exposed to oxidant stresses (hydrogen peroxide and hyperoxia), and survival rates were determined. Results demonstrated a significant resistance to oxidative stress in cells overexpressing catalase when compared to controls. These transfected cell lines will provide important models for further evaluation of the role of catalase in **protecting** cells against the toxic effects of oxygen-derived **free radicals** and their derivatives.

L7 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1990:34302 CAPLUS

DN 112:34302

TI Macrophage-mediated induction of DNA strand breaks in target tumor cells

AU Chong, Yen C.; Heppner, Gloria H.; Paul, Leslie A.; Fulton, Amy M.

CS Dep. Immunol., Michigan Cancer Found., Detroit, MI, 48201, USA

SO Cancer Research (1989), 49(23), 6652-7

CODEN: CNREA8; ISSN: 0008-5472

DT Journal

LA English

AB It was shown previously that macrophages are mutagenic to bacteria and can induce the appearance of drug-resistant variants of murine mammary tumor cells. The present study asks whether inflammatory macrophages can induce lesions in the DNA of cocultured tumor cells and seeks to det. the mediators of this damage. The induction of DNA strand breaks was quantitated by using fluorometric anal. of DNA unwinding. The inflammatory macrophages coincubated with a mammary tumor cell line for 60 min at a 1:1 ratio result in significant nos. of strand breaks in the tumor cell DNA. The degree of damage is equiv. to 300-1200 rads of .gamma.-irradn. Resident (unstimulated) peritoneal macrophages also induce tumor cell DNA strand breaks. However, inhibitor studies reveal quant. and qual. differences in strand breaks induced by inflammatory (elicited) vs. resident peritoneal macrophages. Resident macrophages require a longer induction period (60 min) before breaks are detected, but induce more breaks than do elicited macrophages, which require only a 5-min coincubation period to induce damage. Catalase, which removes H<sub>2</sub>O<sub>2</sub>, protects tumor cells from both macrophage effector populations as does the prostaglandin synthase inhibitor, indomethacin. The **superoxide anion** scavenger, superoxide dismutase, and the lipoxxygenase inhibitor, nordihydroguaiaretic acid, are **protective** only against resident macrophage effects. The metal chelator, o-phenanthroline, provides limited protection for elicited macrophages but induces total DNA breakage in the presence of resident macrophages. These data indicate that the degree of strand breakage is greater for the macrophage population with high arachidonate metab. and low oxidiatve metab. (resident macrophages) and less for the macrophage population with high oxidative and low arachidonate metab. (MVE-2 elicited macrophages). Both metabolites of reactive oxygen and arachidonate are implicated as mediators of this tumor cell DNA damage, with the relevant mediator dependent upon the particular macrophage population under study.

L7 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1984:546289 CAPLUS

DN 101:146289

TI Studies on the **protection** of DNA strand breakage induced by **free radicals**

AU Kim, Won Jin; Oh, Sang Hwan; Kim, Yoon Soo

CS Coll. Med., Yonsei Univ., Seoul, S. Korea

SO Yonsei Uidae Nonmunjip (1984), 16(2), 373-86

DT Journal

LA Korean

AB An expt. was designed to investigate (1) if reactive O metabolites generated in in vitro systems influence DNA breakage, (2) if the destruction is by single radicals or 2 radicals cooperatively, and (3) to det. if **free radical** scavengers and detoxifying-enzyme systems function effectively in **protection** of DNA damage from these reactive O radicals. T4 phage DNA was not damaged by superoxide generated by the xanthine-xanthine oxidase system, and **superoxide dismutase** had no influence on the **DNA** damage. Neither 100 mM H<sub>2</sub>O<sub>2</sub> nor Fe<sup>2+</sup> plus superoxide produced by the xanthine-xanthine oxidase system caused efficient DNA damage. T4 phage DNA was not cleaved by reaction with superoxide and H<sub>2</sub>O<sub>2</sub> (10 mM), but hydroxyl radical generated from 10 .mu.M Fe<sup>2+</sup> and 1 mM H<sub>2</sub>O<sub>2</sub> caused efficient DNA strand breakage, and the degree of strand breakage was proportional to the concn. of H<sub>2</sub>O<sub>2</sub>. About 50% of calf thymus DNA was cleaved by OH.bul. generated from the reaction of 10 .mu.M Fe<sup>2+</sup> and 30 mM H<sub>2</sub>O<sub>2</sub>, and >80% of the DNA was cleaved by 10 .mu.M Fe<sup>2+</sup> and 60 mM H<sub>2</sub>O<sub>2</sub>. The free radical scavengers mannitol and histidine both prevented T4 phage DNA damage from OH.bul. generated by the reaction of 10 .mu.M Fe<sup>2+</sup> and 10 mM H<sub>2</sub>O<sub>2</sub>. The protective effect of 10 mM histidine against DNA damage by OH.bul. was similar to that of 50 mM mannitol. **Catalase** (0.5 units) protected T4 phage **DNA** from OH.bul. generated by 10 .mu.M Fe<sup>2+</sup> and 10 mM H<sub>2</sub>O<sub>2</sub>, and glutathione peroxidase (0.67 .times. 10<sup>-3</sup> units) protected DNA almost completely from damage under the same conditions. The protective effect of **glutathione peroxidase** against **DNA** damage induced by OH.bul. was .apprx.1000-fold stronger than that of catalase. The physiol. role of **catalase** and **glutathione peroxidase** in preventing the **DNA** damage by OH.bul. is significant, as the amt. of enzyme used in this expt. was much lower than cellular levels.

=>